



Regulation of transcription

Regulation of gene expression is vital to allow cells to control the amount and timing of synthesis of their functional products needed at any given point.

Giving cells control over their structure and function, regulation of gene expression is the basis for cellular differentiation, morphogenesis and the versatility and adaptability of any organism.

It's very important to realise that gene transcription is a tightly regulated process that helps the cell to adapt to different and changing environmental contingencies. In other words, gene regulation is a process that lets the cell control the amount and the timing of synthesis of the functional product needed of their functional product at any given time.

Notes

Summary



0m 05s

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Giving cells control over their structure and function, regulation of gene expression is the basis for cellular differentiation, morphogenesis and the versatility and adaptability of any organism.

Purpose

Shape developmental pathways

Respond to environmental stimuli

Adapt to nutritional status to the cell

Key facts

Happens at multiple **stages of development**

Triggered by different (external and internal) **factors**

Happens throughout the **lifespan** of organisms

You can imagine a bacteria that is exposed to a sudden rise in temperature, called heat shock. Then it would make sense that the bacteria manages to express all the genes that help to fight against this heat shock induced cellular damage with so-called heat shock proteins. Gene regulation serves the purpose of having all of these genes then expressed at the same time. Now conversely, if the cell or the bacteria is not in a so-called heat shock state, then it doesn't make sense to use energy to express these genes. In that case, gene regulation helps to shut off these genes to maintain them in a silent state and thereby to save energy. Gene regulation gives cells control over the structure and function, and thereby it forms the basis of cellular differentiation, morphogenesis, and the versatility and adaptability of any given organism. The purpose, thus, is not only to shape developmental pathways, but also to respond to different and changing environmental stimuli and thereby to adapt to the nutritional status of the cell. The key facts to remember are, that gene regulation happens at multiple stages of development. It can be triggered by different both external and internal factors, and it can happen, and it does happen, throughout the lifespan of an organism.

Notes

Summary

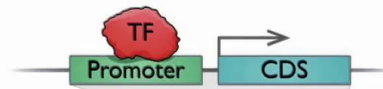


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Regulation of transcription

Scale

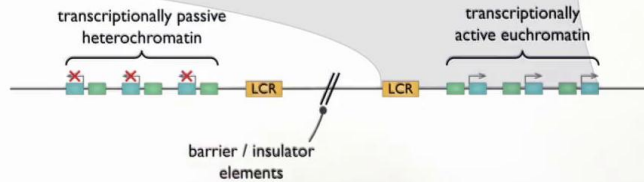
Coding sequence:



Locus:



In between loci:



Glossary

TF - Transcription Factor
CDS - Coding Sequence
LCR - Locus Control Region
GRN - Gene Regulatory Network

The regulation of gene transcription happens at different scales. It happens at the scale of the coding sequence, as we have seen before, by the binding of transcription factors or RNA polymerase to the promoter region of a gene. Furthermore, it can happen at what is called a Locus Control Region. For instance, this would be, all these three genes here would have a similar function that ought to be expressed at the same time and this is being mediated by them being integrated into what is called a Locus Control Region. In the case of the heat shock proteins that I mentioned before, it would make sense to have one Locus Control Region for all heat shock proteins. In the case of Alzheimer's disease, it would make sense to have genes that fight against toxic amyloid beta species to be under the control of one Locus Control Region. Furthermore, then obviously, there can be multiple Locus Control Regions, and these Locus Control Regions can have different functions. Then it's important to separate transcriptionally active Locus Control Regions from transcriptionally passive ones.

Notes

Summary

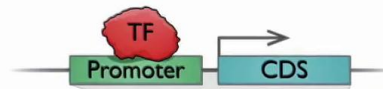


2m 02s

Regulation of transcription

Scale

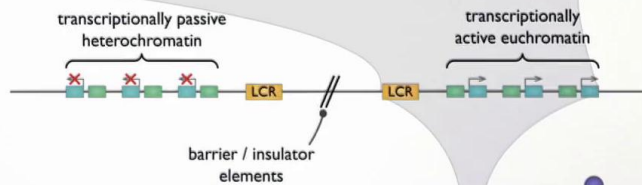
Coding sequence:



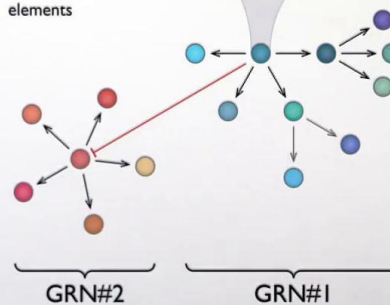
Locus:



In between loci:



On multiple loci at the same time:
Gene regulatory network



Glossary

TF - Transcription Factor
CDS - Coding Sequence
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This is being brought about by various mechanisms, including so-called barrier and insulator elements that clearly separate transcriptionally passive or heterochromatin regions from transcriptionally active or eukromatin regions. If we zoom further out, we can see that gene regulation can occur also at a very distant scale, namely in so-called Gene Regulatory Networks. In the case of heat shock proteins, it would make sense that this Gene Regulatory Network here that we have seen when we zoomed in before would stimulate and positively influence the regulation of other Gene Regulatory Networks that have a similar function. Conversely though, it would also make sense that Gene Regulatory Networks can interact with one another. If Gene Regulatory Network two here has a different function than Gene Regulatory Network one, then it would make sense that Gene Regulatory Network one shuts off the expression of Gene Regulatory Network two. Multiple scales of gene regulation at the coding sequence, at the locus region, in between loci and within what is called a Gene Regulatory Network.

Notes

Summary



3m 18s

Regulation of transcription

Mechanisms

• Pre-transcription

- Chromatin accessibility
- DNA looping
- cis- and trans- remodeling
- Epigenetic modifications

• During transcription

- Activators/repressors
- Combinatorial regulation
- Positive and negative feedback loops

• Post-transcription

- RNA processing
- RNA stability and lifetime – miRNA and siRNA
- Post-translational mechanisms

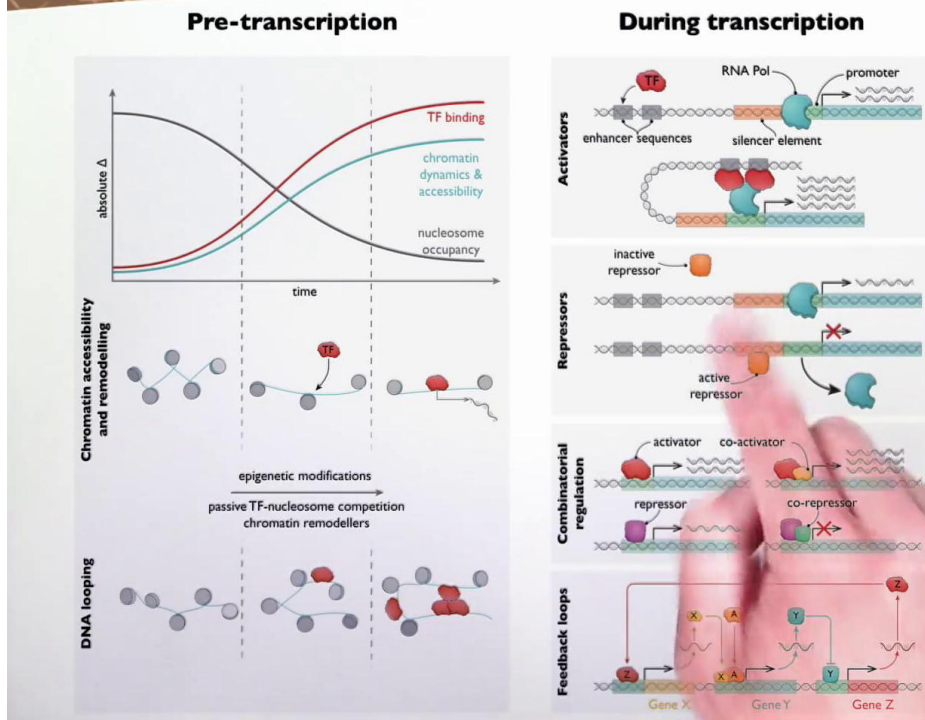
What are the mechanisms of the regulation of gene transcription. The regulation of gene transcription can happen before transcription actually starts. This is being mediated by the accessibility of the chromatin to different transcription factors that is being brought about by DNA looping, by what is called cis- and trans-remodelling, and of course, also by epigenetic modification. Furthermore, it can happen during transcription, where we have the binding on and off of activators and repressors that also influence one another via a combinatorial regulatory mechanism. As we will see, we can have positive and negative feedback loops. Finally, the regulation of gene transcription can happen also post-transcriptionally by a mechanism that we refer to as RNA processing and by the intrinsic RNA stability and the molecular lifetime of RNA molecules that is influenced intrinsically, but also by what is called a micro RNA-mediated degradation of RNA species and by short interfering RNA molecules. Then finally, once translation has happened by so-called post-translational modifications.

Notes

Summary



Regulation of transcription



If we look at the pre-transcription step, we can see that the transcription factor binding is influenced by the chromatin accessibility. Chromatin can be in an open or in a closed state, and this is important to allow transcription factors to bind. Nucleosome occupancy decreases as chromatin accessibility becomes higher. This chromatin accessibility is also depicted on this scale. We can have on the left a very compact or condense structure, and then this switches into a primed or poised state where transcription factors can bind, have access to the DNA and to an active state, transcriptionally active state where transcription factors are bound and do their job in transcribing the DNA. This is being mediated in both directions by epigenetic modifications. Then finally, we can also have what is called the DNA looping. For instance, this region up here where the transcription factor in red is bound, will be brought into proximity to the transcriptional start site down here. Then this will influence and kick off gene transcription. During transcription, we can have the binding of activators to the promoter region of a gene, and we can have the binding of so-called enhancer elements, for instance, by a looping to the promoter region of a gene.

Notes

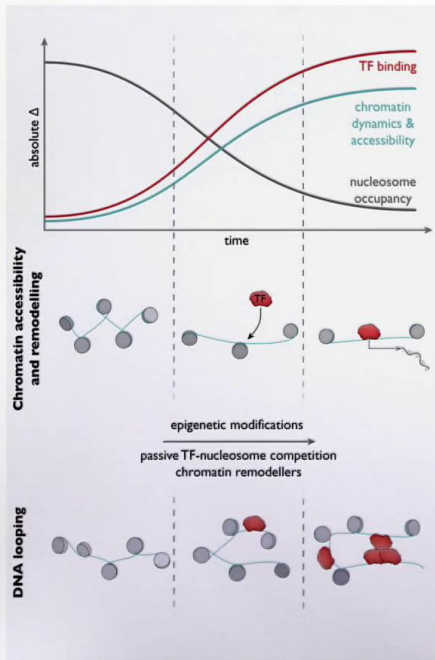
Summary



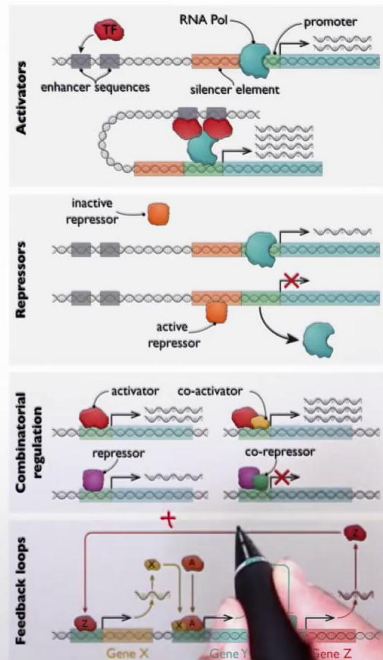
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Regulation of transcription

Pre-transcription



During transcription



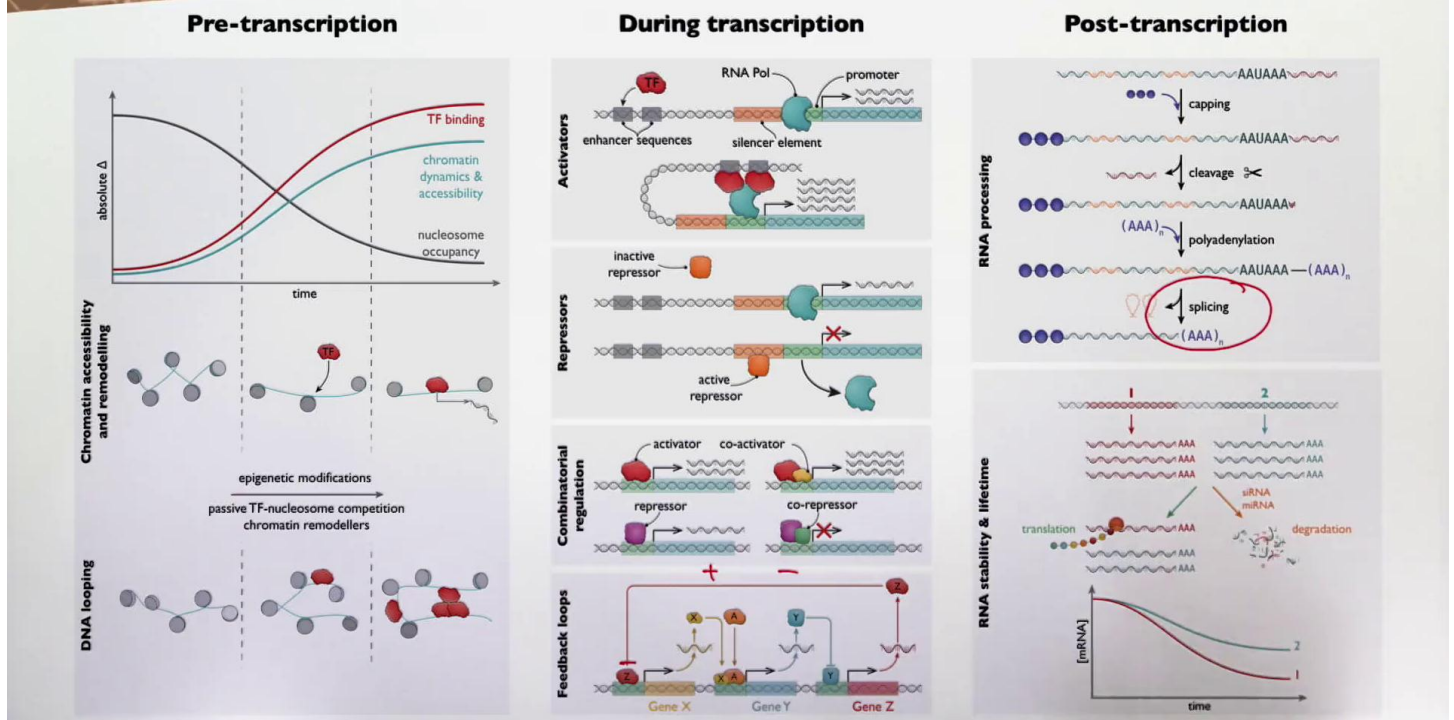
This brings into proximity the transcription factors here to RNA polymerase that is depicted here in blue. Together, this can then influence the rate of gene transcription. Now, of course, at the same time as we as we have activators, we can have repressors that can be inactive because they're not bound. If they bind to what is depicted here in orange, the silencing element, then of course, gene transcription does not occur. Of course, life is not always that easy, but we can have a combinatorial regulation between activators, coactivators, repressors, and co-repressors. This can influence the rate of gene transcription. Finally, what we can also have are so-called feedback loops. In this example, gene X will encode for enhancer element X that binds to and helps the expression of gene Y. Gene Y then expresses protein Y, that will bind to and influence the expression of gene Z. Gene Z can be, in this case, a transcription factor that either positively feedbacks to gene X to stimulate its transcription. This would be the example of a positive feedback loop, or it could be a repressing element, a repressor that binds to the promoter region of gene x and silences its expression.

Notes

Summary



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Feedback loops can either be positive or negative, in which case we would draw a line here. Then the last step of gene regulation can occur post-transcriptionally. By post-transcriptionally, we mean here, once transcription has already started. What we have here is a mechanism that we're going to look at a little bit more in detail, which is called splicing. Then finally, what was already mentioned before, we can have different intrinsic lifetimes of different RNA molecules. In this example here, we have RNA molecule number two that stays longer alive and can have a longer-lasting effect than RNA molecule number one in red, which is more quickly degraded.

Notes

Summary

